REMARKS

This Amendment, filed in reply to the Office Action dated April 17, 2009, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 5, 9 and 10 are rejected. Claim 5 is canceled herewith without prejudice or disclaimer. No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Withdrawn Rejections

Applicants thank the Examiner for withdrawal of the rejection of Claim 5 under 35 U.S.C. § 103.

Claim 9 is Patentable under 35 U.S.C. § 102(b)

On page 3 of the Office Action, Claims 5 and 9 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Haro *et al.* (*Journal of Clinical Investigation*, 2000, 105(2):143-150; hereinafter "Haro #1").

In making the rejection, the Examiner contends that Haro #1 discloses addition of macrophages from MMP-3 null mice to wild-type intervertebral discs, and that such administration resulted in a reduction in wet weight of the discs. The Examiner further contends that macrophages from MMP-3 null mice, while deficient in MMP-3 production, are capable of producing MMP-7. The Examiner thus concludes that "the presence of macrophages from MMP-3 null mice is tantamount to administration of MMP-7 in the absence of MMP-3."

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, to compact prosecution of the Application, Claim 5 is canceled herewith, without prejudice or disclaimer, mooting the rejection of this claim.

Turning to the substance of the rejection as it applies to Claim 9, Applicants strongly, but respectfully, disagree that Haro #1 anticipates Claim 9 as examined.

Specifically, Applicants respectfully point out that Claim 9 recites a method which "consists essentially of directly administering MMP-7 to the affected site of the herniated disc or herniated nucleus pulposus." It is well-settled that the transitional term "consisting essentially of" excludes from the scope of the claim *any* additional component that materially affects the basic and novel characteristics of the claimed invention, in the instant case, these characteristics being *inter alia* HNP degradation. Applicants respectfully point out that, as would be readily appreciated by one of ordinary skill in the art reading Haro #1, disc degradation in the experiments of Haro #1 occurs by the addition and subsequent infiltration of macrophages into the disc, which infiltration is mediated by multi-step macrophage-chondrocyte interactions. That is, the administered macrophages *themselves* materially affect HNP degradation activity, and thus *materially affect the basic and novel characteristics of the claimed invention*. Moreover, not only do the administered macrophages materially affect HNP degradation activity, but Haro #1 actually discloses that HNP degradation is *completely dependent* on the presence of macrophages; on page 147, column 2, Haro #1 discloses that "*in vitro* disc resorption ***required*** macrophage infiltration." (Emphasis added.) Thus, it is clear that the administration of *macrophages* from MMP-3 null mice, *i.e.*, the method of Haro #1, does not constitute administering a composition "consisting essentially of MMP-7," as appears to be the Examiner's

belief,[1] because the disclosed criticality of the macrophages in HNP degradation precludes such an interpretation. As such, Haro #1 does not anticipate Claim 9.

Withdrawal of the rejection is respectfully requested.

Claim 10 is Patentable Under 35 U.S.C. § 103(a)

On pages 3 and 4 of the Office Action, Claim 10 is rejected under 35 U.S.C. § 103 as allegedly being obvious over Haro #1.

In making the rejection, the Examiner acknowledges that Haro #1 does not disclose a method consisting of administering MMP-7 and a pharmaceutically acceptable carrier to the affected site of a herniated disc or herniated nucleus pulposus, as claimed. However, the Examiner contends that one of ordinary skill in the art would readily have administered *just* MMP-7 to the site of a herniated disc because Haro #1 allegedly discloses the importance of MMP-7 in disc resorption, citing page 148, column 1, paragraph 2 ("Macrophage-derived MMP-7, but not MMP-3, was required for disc resorption and macrophage invasion of disc tissue.") Further, the rejection also appears to be predicated on the basis that one of ordinary skill in the art would have understood from Haro #1 that MMP-3 deficient macrophages "consist essentially of MMP-7,"[2] and thus would readily have administered MMP-7 *alone*.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

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[1] While not expressly indicated in the anticipation rejection, the Examiner states on page 4, 3rd paragraph, of the Office Action, under the rejection of Claim 10 under 35 U.S.C. § 103, that "MMP-3 deficient macrophages, which consist[] essentially of MMP-7."

[2] See page 4, 3rd paragraph, of the outstanding Office Action.

Initially, Applicants respectfully point out that, as would readily be appreciated by one of ordinary skill in the art, Haro #1 discloses, through numerous experiments, the *criticality* of the administered macrophages in the disc resorption process characterized therein; one of ordinary skill in the art would readily have appreciated from Haro #1 that chondrocyte- or macrophage-derived MMP-3 *or* MMP-7, is not, in itself, sufficient to mediate disc resorption, but rather that macrophages are necessary, due to the complex interplay between chondrocyte- and macrophage-signaling that results in macrophage infiltration (which is disclosed by Haro #1 to rely on factors produced from both chondrocytes, and macrophages, to chemoattract macrophages to infiltrate the herniated disc to mediate resorption). As a result, it is clear that one of ordinary skill in the art would not have possessed any motivation to administer MMP-7 without macrophages, much less alone, nor would they have possessed any expectation of success in doing so, as is required to maintain the rejection. For at least this reason, Claim 10 is not rendered obvious by Haro #1.

Further, in view of the disclosed criticality of macrophages in the disc resorption process of Haro #1, one of ordinary skill in the art at the time of the invention would readily have recognized that the modification proposed by the Examiner would clearly render the method of Haro #1 inoperable for its intended purpose, *i.e.*, disc resorption; relevant law holds that if a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Thus, for this reason also, Claim 10 is not rendered obvious by Haro #1.

Further, Applicants respectfully submit that Haro #1 represents less pertinent art than that already of record, specifically Haro *et al*. (*Spine*, 1997, 22(10):1098-1104; hereinafter "Haro #2"). With regard to Haro #2, Applicants successfully rebutted the Examiner's presumption of obviousness by demonstrating that MMP-7 was vastly, yet unexpectedly, superior in disc resorption vis-à-vis MMP-3. Thus, Applicants have already demonstrated the non-obviousness of the present invention over more relevant art than that currently cited, and as such, Applicants aver that the non-obviousness of the present invention has already been established on the record.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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